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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 10/070134

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
H 52 437 C3 MD		
International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/FR00/02481	08 September 2000 (08.09.00)	10 September 1999 (10.09.99)

International Patent Classification (IPC) or national classification and IPC
C12Q 1/68

Applicant
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1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13 February 2001 (13.02.01)	11 December 2001 (11.12.2001)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR00/02481

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☒ the international application as originally filed.

☐ the description, pages 1-18, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. 1-15, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig 1/2-2/2, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR 00/02481

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	4-15	YES
	Claims	1-3	NO
Inventive step (IS)	Claims		YES
	Claims	1-15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations

Reference is made to the following documents:

D1: DATABASE EMHUM6 [online] EMBL; ALAIBAC ET AL: MOLECULAR IMMUNOLOGY, Vol. 33, 1996, pages 1035-1038,

D2: WO 97 11162 A

D3: WO 98 44130 A

D4: WO 96 23071 A

D5: ALEKSHUN M ET AL: AN INTERNATIONAL JOURNAL ON GENES AND GENOMES, Vol. 186, No. 2, 28 February 1997 (1997-02-28), pages 227-235

D6: WO 98 59034 A

D7: WO 98 58943 A

D8: US-A-5 786 147

D9: MOLLET C ET AL: MOLECULAR MICROBIOLOGY, (1997 DEC) 26(5) 1005-11.

The claimed priority date of 10.09.1999 can be acknowledged for the subject matter of Claims 1-15. As a result, the document by Renesto et al, cited in the international search report, is not considered to form part of the prior art (PCT Article 33(2)).

1. The subject matter of Claim 1 of the present application does not fulfil the requirements of novelty of PCT Article 33(2).

D1, which relates to the T cell receptor, describes a single-stranded oligonucleotide sequence, Hsz78027, which is homologous to the sequence SEQ ID NO: 1 of the present application over 12 nucleotide motifs.

Document D2 relates to 17-beta-hydroxysteroid hydrogenase and describes an oligonucleotide sequence, T63467 (SEQ ID NO: 57, page 45, line 18) which is homologous to the sequence SEQ ID NO: 2 of the present application over 12 nucleotide motifs.

Document D3 relates to antigenic proteins of *Helicobacter pylori* and describes an oligonucleotide sequence, V45541 (page 15, line 17) which is homologous to the sequence SEQ ID NO: 3 of the present application over 13 nucleotide motifs.

D4, which relates to the field of specific antibodies to the human epitopes, gp39, describes an oligonucleotide sequence, T35996 (SEQ ID NO: 40, page 80, line 39) which is homologous to SEQ ID NO: 4 of the present application over 12 nucleotide motifs.

It follows that the technical features of the subject matter of Claim 1 cannot be considered to be novel (PCT Article 33(2)).

As a result, the subject matter of dependent Claims 2 and 3 cannot be considered to be novel (PCT

Article 33(2)) for the same reasons.

2. The subject matter of dependent Claims 4 and 5 is not inventive (PCT Article 33(3)). The replacement of a nucleotide base with inosine and a mixture of specific oligonucleotides for the detection of a target sequence involves technical features that are well known in this technical field. It follows that said claims are not considered to involve an inventive step.

3. The subject matter of Claim 6 is not inventive (PCT Article 33(3)).

The subject matter of this claim relates to probes for the detection of *Spirochaetales* having the features of the subject matter of Claims 1 to 5.

Probes for detecting *Spirochaetales* are known from the prior art.

Document D5, which relates to the characterisation of *Borrelia burgdorferi*, describes degenerate oligonucleotide sequences that are used for southern hybridisation for the identification of the rpoB gene (page 228, column 1, paragraph 1). A method for identifying the genes of bacteria of the order *Spirochaetales* is already known from D5.

In addition, other documents such as document D6, which relates to nucleotide sequences of *Treponema pallidum* and document D7, which relates to nucleotide sequences of *Borellia burgdorferi*, describe methods for identifying the sequences of said strains (see D6: Claim 6 and D7: Claim 18).

As a result, since the oligonucleotides of SEQ ID NOS: 1 to 4 do not have any technical features that confer any specific effects, the subject matter of Claim 6 cannot be considered to involve an inventive step (PCT Article 33(3)).

3.1 The subject matter of Claims 7 and 8, which are dependent on Claim 6, as well as that of Claim 9 relate to technical features that are considered to be common in the technical field in question. It follows that Claims 7 and 8 are not inventive (PCT Article 33(3)).

4. The subject matter of Claim 10 is not inventive (PCT Article 33(3)).

Document D8, which relates to the detection of enterobacteria, describes the use of the oligonucleotide sequences of the rpoB gene as a genetic marker for identifying and detecting bacteria of the enterobacteria family (column 1, lines 44-50; column 4, line 55 to column 5, line 67).

D9 relates to the same field as D8 and discloses the highly useful use the rpoB gene for the genotypic identification of bacteria (see the abstract). What is more, D9 describes oligonucleotide sequences for the amplification and the detection of the rpoB gene (see Figure 1 and page 1009, column 2, paragraph 2).

It follows that a person skilled in the art, aware of the highly useful use of the rpoB gene to identify enterobacteria that is described in

documents D8 and D9 and the method described in D5, which uses the oligonucleotide sequences for the southern hybridisation of the rpoB gene, would have been prompted to use this rpoB marker sequence, which is also already known for bacteria of the order *Spirochaetales*, see D6 (*Treponema pallidum*), page 427, nt 11930-11980, and D7 (*Borellia burgdorferi)* nt 12760-12810 for the rpoB sequence of said bacteria for the detection of bacteria of the order *Spirochaetales* using nucleotide primers. This does not involve an inventive step (PCT Article 33(3)).

The same observations apply with respect to the subject matter of Claims 12, 14 and 15 and dependent Claims 11 and 13 concerning a procedure for determining the presence of the bacteria of the order *Spirochaetales* using primers and the detection of said bacteria using detection probes and gene therapy probes.

It follows that the technical features of the subject matter of Claims 11-15 cannot be considered to involve an inventive step (PCT Article 33(3)).

Nevertheless, the applicant's attention is drawn to the following point:

The insertion of the definition of "equimolar mixture", set out on page 6, lines 18-24, into Claim 1 could render said claim novel.

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Contrary to the requirements of PCT Rule 5.1(a)(ii), the description does not indicate the relevant prior art disclosed in documents D1-D4 and D6-D8, nor does it cite said documents.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 15 does not fulfil the requirements of PCT Article 6 because the expression "gene therapy probe" is not clear.